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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/650,613	08/27/2003	Vincent Geenen	ULS-001.01	8967

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EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 07/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/650,613	GEENEN, VINCENT	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 16-19* is/are pending in the application.

4a) Of the above claim(s) *1-10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-13 and 16-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of Group II, filed 5/18/06, is acknowledged.

Claims 14 and 15 have been canceled.

Claims 16-19 have been added.

Claims 1-10 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 11-13 and 16-19 are being acted upon.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 10-13 and 16-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention.

Regarding *in vivo* methods (and products intended for *in vivo* use) which rely on previously undescribed and generally unpredictable mechanisms, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166

USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)." The MPEP further states that physiological activity can be considered inherently unpredictable. With these teachings in mind, an enabling disclosure, commensurate in scope with the breadth of the claimed invention, is required.

The instant claims encompass peptides for preventing type I diabetes and inducing tolerance in a subject at risk for developing type I diabetes. Curiously, applicant has chosen to detail some of the difficulties encountered by other researches in attempting to induce tolerance, particularly in human patients. Indeed, applicant has provided numerous references, e.g., Pozzilli, et al. (2000), demonstrating that, while the induction of tolerance would be expected, it simply does not occur. Other unsuccessful examples are known in the art. See for example, *Marketletter* (9/13/99) which teaches the complete failure of tolerance induction in human trials. Both Myloral (for multiple sclerosis) and Colloral (for rheumatoid arthritis) provided successful results in inducing tolerance in animal models, however, both were complete failures in human trials. Also note an additional more recent reference (Goodnow, 2001), wherein the author flatly states, "Obtaining the desired response [tolerance] with these strategies [tolerance induction] is unpredictable because many of these signals [tolerogenic] have both tolerogenic and immunogenic roles," (see the Abstract). The author goes on to teach that while the induction of oral tolerance might be considered "an attractive notion", the method has failed in humans because of the lack of understanding of the mechanisms involved (page 2120, column 2).

A review of the instant specification shows no induction of tolerance and indeed, it is unclear precisely what the single example is intended to demonstrate. It appears that an *in vitro* CD4 response in $DQ8^+$ diabetics to a single IGF-2 peptide was measured. Somehow, the induction of the secretion of IL-10 *in*

vitro is intended to support the induction of *in vivo* tolerance with the essentially unlimited number of peptides and proteins that might be encompassed by the instant claims.

Also note that Claims 11 and 12 would encompass fragments as small as two amino acids. Finally note that no demonstration whatsoever is offered to provide support for a method of preventing diabetes. Clearly then, the brief teachings of the instant disclosure, wherein no *in vivo* nor even relevant *in vitro* data is disclosed, cannot be considered to be enabling for the products of the instant claims.

In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Thus, in view of the quantity of experimentation necessary, the lack of sufficient guidance in the specification, the lack of sufficient working examples, i.e., the specification discloses no data relevant to the induction of tolerance, the unpredictability of the art, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

4. Claims 11, 12 and 16-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Under *Vas-Cath, Inc. v. Mahurkar* , 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession* of the invention, and that the invention, in that context, is whatever is now claimed.

There is insufficient written description to show that Applicant was in possession of an IGF-2 peptide capable of preventing type I diabetes or inducing tolerance in a subject at risk of developing type I diabetes.

Regarding the claimed peptide, said peptide is described by function, but no common structure has been disclosed. Just a single example is disclosed, and it is unclear if it has the

required functional properties. Given the breadth of the claims, it is likely, that the claimed genus of peptides is intended to be quite large. Given the lack of sufficient examples of IGF-2 peptides capable of preventing diabetes of inducing tolerance, it is the Examiner's position that one of skill in the art would conclude that the specification fails to disclose a representative number of species to describe the peptide of the claims. See *Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 11-13 and 16 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by the Sigma Catalog (1994).

The Sigma Catalog teaches a human IGF-2 peptide of at least 50 amino acids suitable for vaccine use (see particularly page 1502).

The reference teaching anticipates the claimed invention.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over the Sigma Catalog (1994) in view of U.S. Patent No. 6,277,375.

The Sigma Catalog has been discussed above.

The reference teaching differs from the claimed invention only in that it does not teach an IGF-2 peptide of at least 75 or at least 100 amino acids.

The '375 patent teaches that the addition of an Ig Fc region to a protein can increase said protein's stability and half-life (see particularly, column 4, lines 28-37 and column 12, lines 52-59).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add an Ig Fc region to the peptide of the Sigma Catalog to increase its stability and half-life as taught by the '375 patent.

9. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over the Sigma Catalog (1994) in view of U.S. Patent No. 6,287,588.

The Sigma Catalog has been discussed above.

The reference teaching differs from the claimed invention only in that it does not teach a PEGylated IGF-2 peptide.

The '588 patent teaches that PEGylation can increase a peptide's stability (see particularly, column 10, lines 57-66).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to PEGylate the peptide of the Sigma Catalog to increase its stability as taught by the '588 patent.

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571)272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

12. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

7/21/06

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Primary Examiner
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